REMARKS

Entry of the foregoing and further and favorable consideration of the subject application are respectfully requested.

As correctly stated in the Office Action, claims 1-33 are pending in the present application. Claims 1-15 and 22-27 stand withdrawn from consideration. Claims 16-21 and 28-33 stand rejected.

By the present amendment, Claims 16-21, 28 and 29 have been canceled, without prejudice to or disclaimer of the subject matter contained therein. New claims 34-37 have been added. Support for these new claims can be found on page 28, ll. 17-23 of the present specification. No new matter has been added. Applicants expressly reserve the right to file a continuation or divisional application on any subject matter canceled by way of the present amendment.

Priority Documents

The Office Action Summary indicates that none of the certified copies of the priority documents have been received. Applicants respectfully submit that the priority documents were filed and acknowledged in grandparent application 08/091,028. Acknowledgement of this matter is respectfully requested.

Claim Objections

Claims 28 and 29 stand objected to as being in improper form. By the present amendment, Claims 28-29 have been canceled, thereby mooting this rejection.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 20-21, 28, 31, and 33 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled. The Examiner asserts that the specification is enabling for *in vitro* production of a megakaryocyte differentiation factor, but not for production of the factor in a transgenic animal. Claims 20, 21, and 28 have been canceled, thereby mooting this rejection as it applies to these claims. This rejection, to the extent that it applies to the remaining claims, is respectfully traversed.

Applicants respectfully submit that the presently claimed invention can be expressed not only in isolated cells, but also in a transgenic animal. The gene can be expressed in a mouse, as follows.

A CMV promoter was linked upstream of a structural gene having the sequence shown in SEQ ID NO: 30 so as to construct an expression plasmid. It was confirmed that the gene in this plasmid is expressed in CHO cultured cells. Next, a 1.2 kb expression unit fragment was taken off from the expression plasmid, and the fragment was microinjected into a fertilized egg of mouse C57BL/J to obtain a transgenic mouse. The transgenic mouse was mated with a wild type mouse to obtain four mouse lines (Tg 620/female), Tg-629/female, Tg667/male, and Tg-694/male, wherein it was confirmed that the introduced gene was transferred to progeny. Of four lines, the line Tg-694/male was used for further experiments. Livers were removed from two heterozygous animals and two wild type litter mates, total RNA was extracted and isolated from each liver, and transcription of the introduced gene was analyzed by RT-PCR. As a result, for two heterozygous animals, the expression was confirmed. For all four lines, the mice were morphologically normal, and they possessed fertilization capabilities.

Thus, the above experiments show that the presently claimed invention can be readily utilized in other transgenic animals, not just isolated cells. Applicants express their willingness to provide the above data in the form of a declaration should the Examiner deem such action necessary.

Applicants respectfully submit that the presently claimed invention is enabled for the full scope of the claims. Withdrawal of this rejection is respectfully requested.

Claims 17, 19-21, and 28-33 stand rejected as allegedly lacking written description. The Examiner asserts that the isolated DNA claimed encompasses numerous structural variants but does not disclose the common attributes or characteristics that define the members of the genus. By the present amendment, Claims 17, 19-21, 28, and 29 have been canceled, thereby mooting this rejection as it applies to these claims. This rejection, to the extent that it applies to the remaining claims, is respectfully traversed.

Applicants respectfully submit that the common attributes may be delineated in part by the representative nucleotide sequence SEQ ID NO: 30 and in part by the amino acid sequence found in SEQ ID NO: 34. Applicants have identified the sequence of SEQ ID NO: 34 and an exemplary nucleotide sequence (*e.g.*, SEQ ID NO: 30) in the genus encoding the amino acid sequence of SEQ ID NO: 34. The nucleotide trimer combinations that encode each individual amino acid are limited and well-known. Once the amino acid sequence was disclosed by Applicants, it is possible to generate a large number of nucleotide sequences that encode this exact same amino acid sequence. Thus, the disclosure of the amino acid sequence conveys the necessary structural information. To require Applicants to recite the

sequence of each possible sequence in the present application and in the claims themselves would be unnecessary and unduly prolix. Moreover, the court in *Enzo* and *Amgen* have recently clarified that not all functional descriptions of genetic material fail to meet the written description requirement. *See Amgen Inc., v. Hoechst Marion Roussel, Inc.*, 65 U.S.P.Q.2d 1385, 1398 (Fed. Cir. 2003); *Enzo Biochem Inc. v. Gen-Probe Inc.*, 63 U.S.P.Q.2d 1609,1613 (Fed. Cir. 2002). Applicants respectfully submit that the Examiner's reference to *In re Deuel* is inapposite to the present situation. While it is true that the disclosure of a protein cannot anticipate or render obvious a particular DNA encoding the protein, here the issue is whether Applicants were in possession of the presently claimed invention, not whether the claimed invention is anticipated or obvious. Given the high level of knowledge of the art and the information provided in the instant specification, Applicants respectfully submit that one skilled in the art would conclude that Applicants were in possession of the presently claimed invention.

Withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. § 102(b)

Claims 17, 19, 21, 30, and 31 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Hermona et al. Claims 17, 19, and 21 have been canceled by the present amendment, thereby mooting this rejection as it applies to these claims. This rejection, to the extent that it applies to the remaining claims, is respectfully traversed.

Claim 30 is directed towards an isolated DNA coding for a megakaryocyte differentiation factor which stimulates differentiation of megakaryocytes, wherein the

DNA hybridizes with a polynucleotide encoding the amino acid sequence of SEQ ID NO:34. Claim 31 is directed towards a method of producing a megokaryocyte differentiation factor comprising culturing a eukaryotic or prokaryotic host cell transformed with an expression vector comprising the DNA (as discussed for Claim 30) under conditions suitable for producing the factor and recovering the factor.

Applicants respectfully submit that one of ordinary skill in the art would consider that it would be difficult for the DNA recited in the claims to hybridize with the DNA of the Hermona et al. publication. As a result of homology analysis of the sequences of the present invention and those of Hermona et al., according to sequence analysis software, DNASIS 3.5 (Hitatch), maximum matching program (Higgins) (Parameters: gap penalty = 5; K-tuple = 4; no. of top diagonals = 5; window size = 5; fixed gap penalty = 10, floating gap penalty = 10), the similarity between the DNA sequence (2213) of megakaryocytopoietin described in Hermona et al. and the DNA sequences of the presently claimed invention is about 22.5%; amino acid sequence similarity between the cited sequence and the amino acid sequence of the presently claimed invention is about 8.3%.

Another sequence homology analysis between the DNA sequence of Hermona et al. and those of the presently claimed invention according to software BLAST2 (NCBI) (Parameters: match = 1; mismatch = -2; gap open = 11; gap extension = 1; x drop off = 50; expect = 10; window size = 3) indicated that "no significant similarity was found."

In light of the above, Applicants respectfully submit that the DNA sequence of Hermona et al. cannot hybridize under any conditions to the DNA of the presently claimed invention. Applicants express their willingness to provide the above

information in the form of a declaration should the Examiner deem such action necessary.

Applicants respectfully submit that the Hermona et al. publication does not disclose each and every element of, and therefore cannot anticipate, the presently claimed invention. Withdrawal of this rejection is respectfully requested.

Double Patenting

Claims 16 and 18 stand rejected under 35 U.S.C. § 101 as allegedly claiming the same invention of Claims 1 and 3 of U.S. Patent No. 5,874,253. Without conceding to the merits of this rejection, and solely in an effort to expedite prosecution, Claims 16 and 18 have been canceled, thereby mooting this rejection.

Claims 17, 19-21, and 28-33 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 5,874,253. Without conceding to the merits of this rejection, and solely in an effort to expedite prosecution, Claims 17, 19-21, 28, and 29 have been canceled, thereby mooting this rejection as it applies to these claims. Applicants respectfully request that this rejection, as it applies to the remaining claims be held in abeyance until the claims of the present application are otherwise allowable.

Conclusions

From the foregoing, further and favorable consideration of the subject application in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

If there are any questions concerning this amendment, or the application in general, the Examiner is respectfully requested to telephone Applicants' undersigned representative so that prosecution may be expedited.

Respectfully submitted,

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